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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/622,452	10/31/2000	David B. Weiner	UPAP-0404	6483
34137	7590	01/10/2007		
COZEN O'CONNOR, P.C. 1900 MARKET STREET PHILADELPHIA, PA 19103-3508			EXAMINER WEHBE, ANNE MARIE SABRINA	
			ART UNIT	PAPER NUMBER
			1633	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/10/2007	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary

Application No.

09/622,452

Applicant(s)

WEINER ET AL.

Examiner

Anne Marie S. Wehbe

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 October 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4, 6, 7, 9-15, 17, 18, 33-36 and 40-52 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-4, 6, 7, 9-15, 17, 18, 33-36 and 40-52 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- ☒ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date 7/25/06
- ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- ☐ Notice of Informal Patent Application
- ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

Applicant's amendment and response received on 10/19/06 has been entered. New claims 46-52 have been added. Claims 1-4, 6-7, 9-15, 17-18, 33-36, and 40-52 are currently pending and under examination in the instant application. An action on the merits follows.

Those sections of Title 35, US code, not included in this action can be found in the previous office action.

#### ***Claim Objections***

Claims 1-4, 6-7, 9-15, 17-18, 33-36, and 40-52 are objected to as reciting non-elected subject matter. The claims are not limited to the elected subject matter of plasmids as the nucleic acid and DR5 as the immunomodulatory protein, but continue to recite numerous non-elected species. As noted in the previous office action, the claims have been examined based on the elected subject matter. It is further noted that the generic claims are not allowable.

#### ***Claim Rejections - 35 USC 112***

The rejection of claims 1-4, 6-7, 9-15, 17-18, and 33-36, and 40-45 under 35 U.S.C. 112, first paragraph, for lack of enablement is maintained over previously pending and new claims 1-4, 6-7, 9-15, 17-18, 33-36, 40-45, 47-48, and 50-52. Applicant's arguments have been fully

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considered but have not found persuasive in overcoming the instant grounds of rejection set forth below.

The previous office action stated that the specification, while being enabling for 1) a method of immunizing a mammal against Influenza comprising co-administering a plasmid DNA encoding Influenza HA and a plasmid encoding DR5 by intramuscular injection and 2) a pharmaceutical composition comprising a plasmid encoding Influenza HA and a plasmid encoding DR5, does not reasonably provide enablement for pharmaceutical compositions comprising a plasmid encoding any immunogen and a plasmid encoding DR5 or for methods of enhancing an immune response or methods of immunizing against any pathogen by administering plasmid(s) encoding an immunogen and DR5. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Please note that while claims 1-4, 6, 9-10, 12-15, 17, 40, and 42-43 are composition or pharmaceutical composition claims, they have been included in this rejection based on the disclosed intended use of the compositions for immunizing a host against disease.

The applicant argues that the data in the previously filed Declaration under 37 CFR. 1.132 by David Weiner shows that CD8+ immune response are enhanced using the claimed invention and that therefore the skilled artisan would recognized the use of a plasmid encoding DR5 in combination with vaccine technology to immunize against an immunogen. The applicant also states that nothing in the cited references suggests that the activity of DR5 is specific for the immunogens tested and could not be used for other immunogens. In response, while the applicant's Declaration provides evidence that DR5 can act to increase antigen specific CD8+ T

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cells when co-administered to muscle with the antigen in the form of plasmid DNA, the declaratory evidence is not commensurate in scope with the breadth of the instant claims as written. While claims 7, 18, and 33 have been amended to recite methods of inducing a CTL response, the recited methods continue to broadly encompass any route of administration, and claim 33 further continues to broadly claim the administration of any nucleic acid molecule, rather than a plasmid or plasmid(s). The cited art of record demonstrates that the type of immune response generated is affected by the route of administration and delivery vehicle (see Abbas et al. and Golding et al.). Further, the remaining method claims continue to read broadly on immunizing an individual against any pathogen or against herpes simplex virus or influenza. The manuscript provided as Exhibit 1 does not teach or suggest that the co-administration of plasmid encoding DR5 has any effect on B cell responses, or any other immune effector cell responses other than CD8+ T cell responses, and the prior art of record teaches that the generation of antigen specific CD8+ T cells does not predictably correlate with a treatment effect on viral infections or cancer (see Yasutomi et al., Erdile et al., and Ertl et al.). It is further noted that while the declaratory evidence did in fact demonstrate a correlation between the generation of Influenza HA specific CTL by intramuscular injection of plasmid encoding HA and DR5, no such correlation was demonstrated for HIV antigen specific CTL and the cited prior art of record clearly teaches that immunization against HIV was considered highly unpredictable at the time of filing (see Fox, and Klein et al.).

Therefore, in view of the state of the art of generating therapeutic immune responses at the time of filing, the lack of specific guidance provided by the specification for using DR5 to enhance immune responses, the limitation of the declaratory evidence to a showing that DR5 can

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enhance CD8+ T cell responses to viral antigens using intramuscular injection, the art recognized unpredictability in immunizing against any disease by generating a CD8+ T cell response, and the breadth of the claims, it would have required undue experimentation to practice the scope of the invention as claimed.

The rejection of claim 41 under 35 U.S.C. 112, second paragraph, for indefiniteness is withdrawn in view of the amendment to claim 41.

***Claim Rejections - 35 USC 102***

The rejection of claims 1-3, 6, and 12 under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 6,417,328 (7/9/02), hereafter referred to as Alnemri, is maintained. Applicant's arguments have been fully considered but have not been found persuasive in overcoming the rejection of record for reasons of record as discussed in detail below..

The applicant reiterates their arguments that Alnemri et al. does not teach the limitation that the plasmid or plasmid compositions are "pyrogen-free", and therefore does not anticipate the claims as amended. This argument was addressed in detail in the previous action, the relevant sections of which are included below for applicant's convenience.

Alnemri et al. specifically teaches the pharmaceutical use of plasmids encoding DR5 to treat disease and further teaches that the pharmaceutical composition is "a sterile aqueous solution that contains no materials in addition to the active ingredients and water or physiological saline (Alnemri et al., columns 22-23, particularly column 23, lines 12-20, emphasis added).

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Thus, while Alnemri et al. does not specifically use the word “pyrogen-free”, Alnemri et al. discloses compositions that are sterile and do not contain material other than the active ingredient, i.e. the plasmid encoding DR5, and water or physiological saline. Such a sterile composition is inherently “pyrogen-free”. While the applicant further argues that “sterile” does not equal “pyrogen free” and that something can be sterile and yet pyrogenic, this argument is not persuasive as Alnemri et al. clearly teaches that in addition to being sterile the pharmaceutical compositions do not contain material other than the active ingredient and water or physiological saline. Since none of the plasmid itself, water, or physiological saline is pyrogenic, the composition as taught by Alnemri et al. is “pyrogen free”.

The applicant further reiterates their argument that Alnemri et al. only teaches the use of the plasmid encoding DR5 and the immunogen LacZ or the combination of the plasmid encoding DR5 and the plasmid encoding CrmA or Flame in *in vitro* assays and that the teachings for making a sterile aqueous solution in columns 22-23 do not apply to these plasmid(s) as the teachings in columns 22-23 refer to pharmaceutical preparations for the treatment of disease and the Alnemri specification does not teach the administration of immunogens with DR5. Again, this argument was addressed in detail in the previous action, the relevant sections of which are included below for applicant’s convenience.

The disclosure in column 22 refers to “expressible nucleic acids encoding DR5”. The plasmids exemplified in columns 27-28 are in fact expressible nucleic acids. Alnemri et al. does not teach that the expressible nucleic acids only encode DR5. As such, since the Alnemri specification broadly teaches to prepare “expressible nucleic acids encoding DR5” as sterile aqueous solutions that do not contain any material other than the nucleic acid, water or

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physiological saline, the teachings in column 22 to prepare sterile aqueous solutions of the nucleic acids reads on the particular plasmids disclosed in the examples regardless of whether they were actually used in *in vitro* experiments. Therefore, the rejection of record is maintained.

### ***Claim Rejections - 35 USC § 103***

The rejection of claims 1-3, 6, and 12 under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,417,328 (7/9/02), hereafter referred to as Alnemri, in view of U.S. Patent No. 5,693,622 (12/2/97), hereafter referred to as Wolff et al. is maintained. Applicant's arguments have been fully considered but have not been found persuasive in overcoming the rejection of record for reasons of record as discussed in detail below..

The applicant argues that there is no motivation to make a pyrogen free plasmid or composition in either Alnemri or Wolff, since neither references teaches or suggests the immuno-enhancing effects of DR5. In response, it is first noted that the claims under rejection are product claims. The fact that applicant has recognized another advantage which would flow naturally from following the teachings and suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). It is reiterated from the last office action that since the Alnemri specification broadly teaches to prepare "expressible nucleic acids encoding DR5" as sterile aqueous solutions that do not contain any material other than the nucleic acid, water or physiological saline, the teachings in column 22 to prepare sterile aqueous solutions of the nucleic acids reads on the particular plasmids disclosed in the examples, which include a single



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plasmid encoding DR5 and the bacterial pathogen immunogen LacZ or the combination of a plasmid encoding DR5 and a plasmid encoding CrmA or Flame, regardless of whether they were actually used in *in vitro* experiments versus *in vivo* methods. Thus, in view of teachings of Alnemri et al. to prepare a sterile pharmaceutical composition comprising a plasmid(s) encoding DR5 for administration to a mammal, and the teachings of Wolff et al. for standard methods of preparing plasmid DNA for *in vivo* administration, it would have been *prima facie* obvious to the skilled artisan at the time of filing to use the standard methods taught by Wolff et al. to prepare the plasmids encoding DR5 and an immunogen taught by Alnemri et al.. Further, based on the standard nature of cesium chloride purification, and the high level of skill in the art of molecular biology at the time of filing, the skilled artisan would have had a reasonable expectation of success in producing a pyrogen-free composition containing the plasmid(s) taught by Alnemri et al. using the purification method taught by Wolff et al. Finally, regarding applicant's argument that the use of DR5 results in an "unexpected result" of enhanced immune response, it is reiterated that the claims under rejection are simply product claims, not method claims, and the references need to provide the same motivation for making the plasmid(s) as applicant. Therefore, the rejection of record is maintained.

No claims are allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. If the examiner is not available, the examiner's supervisor, Joseph Woitach, can be reached at (571) 272-0739. For all official communications, **the new technology center fax number is (571) 273-8300**. Please note that all official communications and responses sent by fax must be directed to the technology center fax number. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737. For any inquiry of a general nature, please call (571) 272-0547.

The applicant can also consult the USPTO's Patent Application Information Retrieval system (PAIR) on the internet for patent application status and history information, and for electronic images of applications. For questions or problems related to PAIR, please call the USPTO Patent Electronic Business Center (Patent EBC) toll free at 1-866-217-9197.

Representatives are available daily from 6am to midnight (EST). When calling please have your

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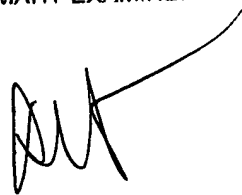
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application serial number or patent number available. For all other customer support, please call the USPTO call center (UCC) at 1-800-786-9199.

Dr. A.M.S. Wehbé

ANNE M. WEHBE' PH.D  
PRIMARY EXAMINER

A handwritten signature in black ink, appearing to be 'AMW', with a long, sweeping horizontal line extending to the right.